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FORMULATION AND *IN VITRO* DISSOLUTION STUDIES OF SALBUTAMOL

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ABSTRACT

Salbutamol is a potent anti-asthmatic agent, is a short-acting β_2-adrenergic receptor agonist act. In the present study, an attempt has been made to prepare fast dissolving tablets of Salbutamol in the oral cavity with enhanced dissolution rate and to achieve better patient compliance. The tablets were prepared with four superdisintegrants e.g., Sodium starch glycolate, Cross-povidone, Cross-carmellose sodium, Pregelatinized starch by direct compression method. The pre-compression parameters of mixed blend were examined for angle of repose, bulk density, tapped density, Compressibility index and Hausner's ratio. The tablets were evaluated for hardness, friability, weight variation, disintegration time, dissolution rate, content uniformity and drug content. It was concluded that the fast dissolving tablets with proper hardness, rapidly disintegrate with enhanced dissolution can be made using selected superdisintegrants. Among all formulations, batch D4 was considered as best since it showed enhanced dissolution, which leads to improved bioavailability, improved effectiveness and hence better patient compliance.

INTRODUCTION: Asthma is an inflammatory disorder that results in the obstruction of air pathways and causes difficulty in breathing [3]. Amongst the currently available means of treatment, oral dosage forms are associated with lag time and delayed onset of action. However, aerosol and parentral have rapid onset of action but strongly affect patient compliance.

Thus, an attempt was made to improve the onset of action of bronchodilator used commonly in treatment of asthma. It is always the aim of a scientist or a dosage form designer to enhance the safety of a drug molecule while maintaining its therapeutic efficacy. Recent advances in Novel Drug Delivery Systems (NDDS) aim for the same by formulating a dosage form, convenient to be administered so as to achieve better patient compliance.

Pharmaceutical technologists have put their best efforts to develop a Fast Dissolving Drug Delivery System [4].

Tablets that disintegrate or dissolve rapidly in the patient's mouth are convenient for children, the elderly and patients with swallowing difficulties, and in situations where potable liquids are not available [5]. Salbutamol is a direct acting sympathomimetic with predominantly -adrenergic activity (β2 -agonist).

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It is an ester pro-drug of β2 adrenergic agonist terbutaline. In the present study, an attempt had been made to prepare fast dissolving tablets of Salbutamol in the oral cavity with enhanced dissolution rate & hence improved patient compliance.

MATERIAL AND METHODS: Salbutamol was obtained as gift sample from Granules Pharmaceuticals Ltd., Hyderabad, AP; Sodium starch glycolate, Cross carmellose sodium, Cross-povidone, Microcrystalline cellulose, Pregelatinised starch were procured from HCS, Hyderabad and all other chemicals/ Solvents used were of AR grade.

Preparation of mixed blend of Drug and Excipients: All the Ingredients were passed through mesh # 60. Required quantity of each ingredient was taken for each specified formulation (listed in the **Table 1**) and all the ingredients were co grind in mortar and pestle (6). The powder blend was evaluated for flow properties such as Bulk density, Tapped density, compressibility index, Hausner's ratio.

Compression of Tablets: The ingredients listed in **Table 1** (except magnesium stearate) were mixed homogenously and cogrinded in a mortar and pestle. Finally, magnesium stearate was added and mixed for 5 min. The mixed blend of drug and excipients was compressed using 10 station rotary punch tablet machine (Karnavati- mini press) to produce convex faced tablets weighing 120 mg each with a diameter of 8 mm. A minimum of 50 tablets were prepared for each batch [7].

Physical characterization of Fast Dissolving Tablets: The formulations were evaluated for weight variation, thickness, friability, hardness, disintegration time, content uniformity, drug content (assay) [the data is presented in **Table 3**] and *in vitro* dissolution study.

Weight variation: Weight variation was done by selecting 20 tablets randomly and weighing individually. Average weight was calculated and the weight of individual tablet was compared with it.

Thickness: The thickness was measured using Vernier Caliper and expressed in mm.

Friability: Friability test was performed using a Roche friability testing apparatus. It is performed to access the effect of friction and shocks which may often cause tablet to chip, cap or break. This device subjects a number of tablets to the combine effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm, dropping the tablets at a distance of 6 inches with each revolution. Pre-weighed tablet sample is placed in friabilator which is then operated for 100 revolutions. The tablets are then dusted and re-weighed. The % friability was measured using following formula: % F= [(W-W0)/W0] X 100 Where; % F = Friability in percentage, W = Initial weight of tablet, W0= Weight of tablet after test [8].

Hardness: The strength of tablet is expressed as tensile strength (Kg/cm^2). The tablet crushing load, which is the force required to break a tablet into halves by compression. It was measured using a tablet hardness tester (Monsanto hardness tester) [9].

Disintegration time: One tablet was placed in each of six tubes of disintegration test apparatus. The test was carried out at 37±2˚C according to USP XXII. Disintegration test apparatus was used without disc. Time required for complete disintegration of tablet fragments through sieve (# 10) was considered as a disintegration time of tablet.

Estimation of Drug Content in Fast Dissolving Tablets: Dissolve 0.320 g in 50 ml of alcohol R and add 5 ml of 0.01 M HCl acid. Carry out potentiometric titration using 0.1 M NaOH. Read the volume added between the two points of inflexion. 1ml of 0.1 M NaOH = 40.39 mg of Salbutamol.

Content Uniformity: The same procedure was followed for content uniformity testing as described under assay procedure for 10 dosage units.

***In vitro* Dissolution studies:** The *in vitro* dissolution study was carried out in USP dissolution test apparatus Type 2 (Electrolab, India). The dissolution medium consisted of phosphate buffer (pH 6.8).An amount of 900 ml of the dissolution fluid was used at 37±0.5^{o}C with stirring speed of 50 RPM. Samples were withdrawn at 1 to 10 minutes, at the time interval of 1 min by replacing with same dissolution medium and samples were analyzed by measuring the absorbance at 265 nm by UV spectrophotometer [1, 10].

TABLE 1: COMPOSITION OF SALBUTAMOL FAST DISSOLVING TABLET

Ingredients	D1	D2	D3	D4	D5	D6	D7	D8
Salbutamol	10	10	10	10	10	10	10	10
Mannitol	50	50	50	50	50	50	50	50
Microcrystalline cellulose	45	40	45	40	45	40	45	40
Pregelatinized Starch	5	10	--	--	--	--	--	--
Cross-povidone	--	--	5	10	--	--	--	--
Cross-carmellose sodium	--	--	--	--	5	10	--	--
Sodium starch glycolate	--	--	--	--	--	--	5	10
Cabosil	3	3	3	3	3	3	3	3
Magnesium Stearate	2	2	2	2	2	2	2	2
Aspartame	5	5	5	5	5	5	5	5
Vanilla	QS	QS	QS	QS	QS	QS	QS	QS
Average weight	120mg	120mg	120mg	120mg	120mg	120mg	120mg	120mg

TABLE 2: PRECOMPRESSION BLEND CHARACTERIZATION

Parameters	D1	D2	D3	D4	D5	D6	D7	D8
Bulk Density(g/ml)	0.398	0.421	0.527	0.421	0.502	0.511	0.421	0.367
Tapped Density (g/ml)	0.454	0.496	0.571	0.468	0.582	0.535	0.438	0.412
Compressibility Index (%)	12.33	15.12	7.71	10.04	13.75	4.49	3.88	10.92
Hausner's Ratio	1.14	1.18	1.08	1.11	1.16	1.05	1.04	1.12
Angle of repose	28.5	29.6	27.8	29.4	28.3	27.6	29.4	29.8

TABLE 3: RESULTS OF POST COMPRESSION PARAMETERS OF SALBUTAMOL

Evaluation	D1	D2	D3	D4	D5	D6	D7	D8
Weight variation (mg)	120 ± 1	119 ± 2	119 ± 2	121 ± 1	120 ± 1	121 ± 1	121 ± 1	119 ± 2
Thickness (mm)	3.42±0.02	3.51±0.01	3.49±0.01	3.57±0.03	3.67±0.02	3.43±0.02	3.49 0.03	3.45±0.01
Friability (%)	0.61	0.54	0.59	0.53	0.67	0.64	0.51	0.58
Hardness (Kg/cm^2)	3.1 ± 0.2	3.5 ± 0.2	3.7 ± 0.1	3.3 ± 0.3	3.1 ± 0.3	3.5 ± 0.1	4.1 ± 0.2	3.9 ± 0.3
Disintegration Time (sec)	54 ± 2.1	50 ± 1.18	20 ± 2.4	17 ± 2.14	30 ± 1.16	26 ± 1.18	35 ± 1.11	30 ± 3.1
Content uniformity (%)	96.1±1.12	96.7±1.21	98.4±1.14	97.4±1.16	92.5±1.11	96.4±1.21	99.7±1.32	93.7±1.24
Assay (%w/w)	99.7	99.85	98.9	98.7	99.4	98.5	101.1	99.5

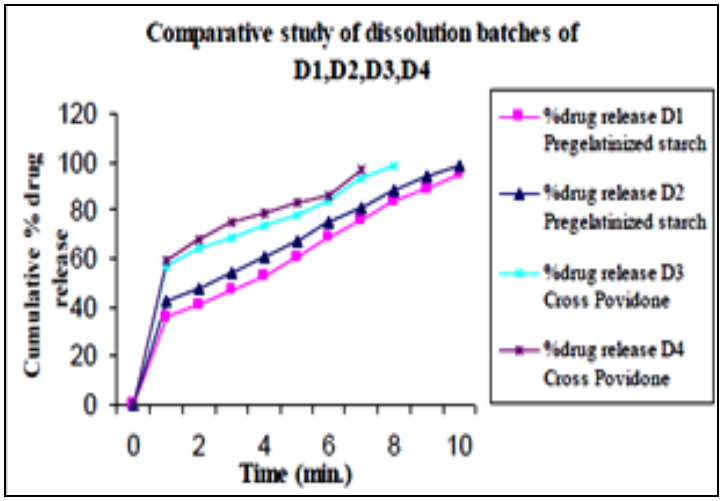

FIG: 1. DISSOLUTION PROFILE OF TABLET PREPARED USING PRE GELATINIZED STARCH AND CROSS-POVIDONE

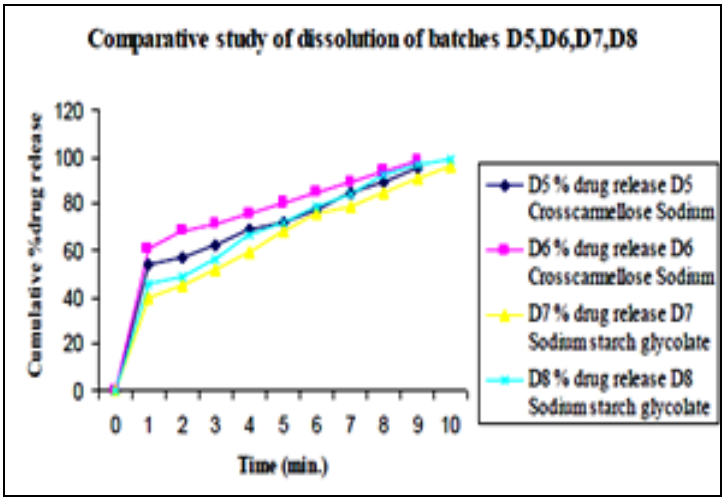

FIG: 2. DISSOLUTION PROFILE OF TABLET PREPARED USING CROSS CARMELLOSE SODIUM STARCH GLYCONATE

The order of enhancement of the dissolution rate with various superdisintegrants was found to be Cross-povidone > Crosscarmellose > Sodium starch glycolate > Pregelatinized starch. It was concluded that fast disintegrating tablets of Salbutamol can be successfully prepared using selected superdisintegrants in order to improve disintegration/dissolution of the drug in oral cavity & hence better patient's compliance & effective therapy [11, 16].

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